

REMARKS

I. Status of the Claims

Claims 1-30 and 35-38 are pending in the application. Claims 35-37 stand withdrawn. Claims 1-30 and 38 have thus been examined as stand and rejected under 35 U.S.C. §102 and §103 over U.S. Patent 6,152,964 (“the ‘964 patent”), optionally in combination with Long *et al.* The specific grounds for rejection, and applicants’ response thereto, are set out in detail below.

II. Rejection Under 35 U.S.C. §102 Over U.S. Patent 6,152,964

Claims 19, 22-28 and 38 stand rejected under §102(a) or (e) over the ‘964 patent. The ‘964 patent is said to disclose “globular structures” or “nodules” which, in the absence of evidence to the contrary, are believed to be the same as the instantly claimed bone spheroids. Applicants traverse.

The nodules described in the ‘964 patent cannot, under any stretch of the imagination, be construed as similar to, much less the same as, the spheroids of the claimed invention. The reasons for this conclusion (as supported in the declaration of Dr. Michael Long under 37 C.F.R. §1.132) is as follows:

- In the ‘964 patent, FIGS. 1 and 4 show scanning electron micrographs of the “globular structures” that the examiner equates with bone spheroids of the present invention. Thus, by definition, these are sub-microscopic, admittedly 0.2-1 μm in diameter. Bone spheroids, on the other hand, comprise 10,000 to 1,000,000 cells, and thus are much larger. Long Declaration at para. 5.
- Another point of distinction is that the ‘964 patent requires use of undifferentiated bone marrow cells. In stark contrast, the present application starts with

undifferentiated bone cells *that are specifically isolated away from bone marrow cells*. Thus, the examiner is quite incorrect in stating that the '964 patent describes "the culture of bone precursor cells. This is strong, if not conclusive evidence, that bone nodules are not bone spheroids. Long Declaration at para. 7.

- Additional evidence of that bone spheroids are *not* the same that the nodules in the '964 patent is provided by what is *not* required in the production of the former, but *is* required in the production of the latter. In the '964 patent, a substrate is required for cell growth, whereas bone spheroids do not. In fact, one of the distinct advantages of the present invention is that spheroids create tissue like aggregates, obviating the need for structural support. Long Declaration at para. 4.
- Still a further point of distinction is the need, when growing the nodules of the '964 patent, for ascorbic acid, β -glycerol phosphate and dexamethasone, none of which are required for spheroid formation. Long Declaration at para. 6.

In light of the foregoing, applicants respectfully request reconsideration and withdrawal of the rejection.

III. Rejection Under 35 U.S.C. §103 Over U.S. Patent 6,152,964

Claims 1-9, 17 and 18 stand rejected under §103 over the '964 patent. The '964 patent is cited as above, as well as for teaching various additional limitations in the rejected claims. Thus, it is argued that claims 1-9, 17 and 18 are, in fact, anticipated, but "in the alternative, the disclosure of the use of 'synthetic serum' and the teaching of both allogenic and autologous cell sources would motivate one of ordinary skill in the art ... to select an appropriate serum free

medium and the specific source of the cells for the practice of the invention.” Applicants traverse.

The basis for this rejection, in one significant aspect, is the assumption that the nodules or globules of the ‘964 patent are the same as the bone spheroids of the present invention. However, as explained in detail above, this assumption is incorrect. To summarize: (a) the nodules are far smaller and much less bone-like than spheroids, (b) bone nodules are derived from bone marrow cells, whereas bone spheroids are not; (c) nodules require a substrate for growth, which spheroids do not; and (d) nodules are not produced in the absence of ascorbic acid, β -glycerol phosphate and dexamethasone, whereas bone spheroids are. Together, this evidence indicates that the ‘964 patent does not teach the bone spheroids as presently claimed. As such, the rejection is improper as the prior art fails to disclose each limitation of the claimed invention.

In light of the foregoing, applicants respectfully request reconsideration and withdrawal of the rejection.

IV. Rejection Under 35 U.S.C. §103 Over U.S. Patent 6,152,964 and Long *et al.*

Claims 10-16, 20-22, 25, 29 and 30 stand rejected under §103 over the ‘964 patent in view of Long *et al.* The ‘964 patent is cited as above. The Long *et al.* paper is said to teach various growth factors, conventional cell separation/purification techniques, and conventional implantation carriers. Applicants traverse.

Once again, applicants submit that the rejection is flawed at its very basis – that the ‘964 patent teaches bone spheroids. This is *not* the case, and the Long *et al.* reference does not cure

the fact that *no* reference teaches bone spheroids as now claimed. As such, this rejection too fails as the cited art does not disclose each limitation of the claimed invention.

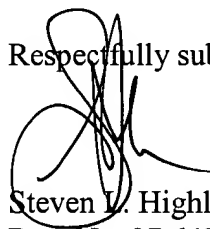
In light of the foregoing, applicants respectfully request reconsideration and withdrawal of the rejection.

V. **Conclusion**

In light of the foregoing, applicants respectfully submit that all claim are in condition for allowance, and an early notification to that effect is earnestly solicited. The examiner is invited to contact the undersigned at the telephone number listed below with any questions, comments or suggestions relating to the referenced patent application.

Please date stamp and return the enclosed postcard as evidence of receipt.

Respectfully submitted,



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